SECTION-I

INTRODUCTION

Research programs for the discovery of new drugs and for improving the evolution criteria are under way in many laboratories. In addition knowledge of specific constituents of the mycobacterium cell and their biochemical roles has become advanced considerably in the recent years and may permit a more rational approach to the design of new drug action on specific targets. Also recent improvements in understanding the mechanism of drug action and its resistance to them may be used as a basis for designing new and better weapons to fight against the mycobacterial diseases.

Heterocyclic compounds have great applicability in pharmaceutics as they have specific chemical reactivity and provide false synthons in biosynthetic process or block the normal functioning of biological receptors. The inhibition of amide resonance resulting in more susceptibility of β-lectam to nucleophile is considered at least in part responsible for antibacterial property, apparently by acetylating transpeptidase and thus inhibiting bacterial cell wall biosynthesis.

Mesoionic compounds are five membered heterocyclic conjugated betains. They are distinct types of heterocycles which belongs to the class of non-benzenoid aromatics. Mesoionic compounds are defined as "five membered heterocycles which cannot be satisfactorily represented by any one covalent or dipolar structure, but only as hybrids of polar structures and they possess a sextet of electrons".[1] The heterocyclic atom vit. Sydnone bear a fractional positive charge which is balance by a corresponding partial negative charge located on exocyclic atom or group of atoms covalently attached to the ring through a carbon atom.[2] They are derivatives of 1,2,3-oxadiazole. The IUPAC name of sydnone is 1,2,3-oxadiazolium-5-olates.

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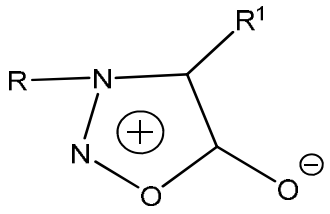
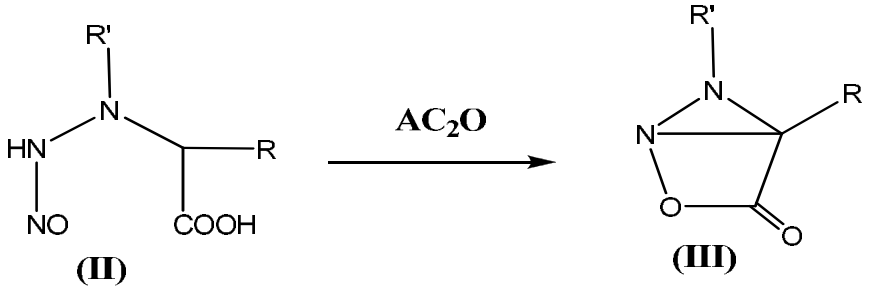
At present the most frequently 'mesoionic' structure of sydnone (I) used was proposed by Baker and Ollis.[3]



(I)

A ± symbol in the fig. (I) was adopted to represent electronic distributions for mesoionic compounds.[4]

The lactone, which is a 1,2,3-oxadiazole-5-one heterocycle was named as "Sydnone" in honour of University of Sydney (**Sydn**ey + lact**one**) where it was prepared for the first time by Earl and Mackney in 1935. Earl and Mackney[5] reported that treatment of *N*-nitroso-*N*-phenylglycine (structure II, R=H, R'=Ph) with acetic anhydride afforded a neutral, anhydro derivative to which the bicyclic structure (structure III, R=H, R=Ph) was assigned.



(II) **(III)**

Sydnone is a typical mesoionic compound and its chemical properties are unique. Sydnone compounds seem to be fairly different from other aromatic compounds in both reactivity and stability.[6]

Sydnone ring undergoes substitution with a wide variety of electrophiles, at 4th position. Some fundamental aromatic reactions such as bromination,[7] nitration,[8] acylation,[9] sulfonation[10] and functionalization of

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various functional groups, such as phosphino, silyl, alkyls, halides etc[11] also occur at this position of the sydnone ring.[12]

Many sydnone compounds have been found to have biological and pharmacological activities. A vast array of sydnone derivatives have been found to show variety of biological properties, such as antimalarial,[13] antiinflammatory,[14] antiarthritic, analgesic,[15] antimicrobial,[16] antitumour,[17] antioxidant[18] and fungicidal.[19] Sydnone derivatives also show significant response of coronary dilation test, collagen induced platelet aggregation inhibition, local anaesthetic, muscle relaxation and moderate cardiotropic activity.[20]

Chalcones are a class of privileged structures that have a wide range of biological properties.[21] An area of particular interest is their potential as anticancer agent.[22] For which several modes of action have been proposed, several oxygenated chalcones and bischalcone are reported to have antimalarial agent.[23] Also literature survey revealed that amino chalcones and corresponding bi-heterocyclic derived from furan enhanced biological activity.[24]

Isoxazole is five membered heterocyclic compounds having two hetero atoms: oxygen at position 1 and nitrogen at position 2. In 1888, L. Claisen[25] reported important contribution to the chemistry of isoxazoles for a product from the reaction of 1,3 diketone with hydroxylamine. Isoxazoles derivatives possess remarkable pharmaceutical importance and biological activities such as anticancer,[26] muscle relaxan,[27] anticholestermic,[28] insecticidal,[29] nematocidal[30] etc.

Benzodiazepines are characterized by their possession of fused benzene ring with seven membered heterocyclic ring containing amino group at five position and nitrogen, sulphur or oxygen at one position with double bond in

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between 4th carbon and 5th nitrogen atom. Considerable research has been undertaken to extend the activity and reduce toxicity of benzodiazepines. The specific biological activities to benzoheterozepines have been summarized as antipyretic, antidepressant,[31] centralnervous stimulatin agent,[32] tranquilizer,[33] etc.

The chemistry of pyrazoline was reviewed by jarobe in 1967. 2-pyrazoline consist a unique class of five member nitrogen heterocycle. From the literature survey 2-pyrazolines are better therapeutic agents. They possess valuable bioactivities like antidepressant,[34] antidiabetic[35] anti-HIV, antioxidant,[36] antitumor[37] etc.

Cyanopyran is a doubly unsaturated six membered ring system with single oxygen as hetero atom. The two double bonds may be conjugated as α or 1,2-pyran or isolated as in γ or 1,4-pyran. Cyanopyrans have resulted in many potential drugs and are known to possess a broad biological spectrum such as antipyretic,[38] cytotoxic,[39] anticoagulant, antifungal,[40] etc.

Cyanopyridine with different functional groups, exhibit wide range of applications in the field of medicine, agriculture and dyes. Most of cyanopyridine derivatives are synthesized by manipulation of pyridine and its simple homologues in a manner similar to chemistry of the benzenoid. cyanopyridine derivatives reported to be active as antimicrobial,[41] antiviral, CNS depressant,[42] antitubercular,[43] antiinflammatory, antihypertensive[44] etc.

In the light of the above observations, the present research work reports the synthesis of chalcone, isoxazole, benzodiazepine, pyrazoline, cyanopyran and cyanopyridine derivatives containing sydnone moiety.

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SECTION-II

EXPREMENTAL

SCHEME-I: 4-(*N*-(4-(3-(substitutedphenyl)acryloyl)phenyl) sulfamoyl)-3- *p*-tolyl-sydnone

The title compounds were prepared via several steps such as esterification, hydrolysis, nitrosation, cyclisation, chlorosulfonation etc.

3-*p*-tolyl-sydnone was prepared by standard method. 4-(chlorosulfonyl)-3-*p*-tolyl-sydnone was synthesized using chlorosulphonic acid and condensed with *p*-aminoacetophenone to get sulfamoyl derivative of sydnone which on treatment with different substituted aldehyde afforded title compounds.

SCHEME-II: 4-(*N*-(4-(5-(substitutedphenyl)isoxazol-3-yl)phenyl) sulfamoyl)-3-*p*-tolyl-sydnone

The title compounds were synthesized by 4-(*N*-(4-(3-phenylacryloyl) phenyl)sulfamoyl)-3-*p*-tolyl-sydnone condensed with hydroxylamine hydrochloride in the presence of sodium acetate in acetic acid.

SCHEME-III: 4-(*N*-(4-(2-(substitutedphenyl)-5a,9a-dihydro-1*H*-benzo[b] [1,4]diazepin-4-yl)phenyl) sulfamoyl)-3-*p*-tolyl-sydnone

The title compounds were prepared by cyclization of 4-(*N*-(4-(3-phenyl acryloyl)phenyl)sulfamoyl)-3-*p*-tolyl-sydnone with *o*-phenylenediamine and sulphuric acid.

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SCHEME-IV: **4-(*N*-(4-(5-(substitutedphenyl)-4,5-dihydro-1*H*-pyrazol-3-yl)phenyl)sulfamoyl)-3-*p*-tolyl-sydnone**

The title compounds were prepared by condensation of 4-(*N*-(4-(3-phenylacryloyl)phenyl)sulfamoyl)-3-*p*-tolyl-sydnone and hydrazine hydrate.

SCHEME-V: **4-(*N*-(4-(6-amino-4-(substitutedphenyl)-5-cyano-4*H*-pyran-2-yl)phenyl)sulfamoyl)-3-*p*-tolyl-sydnone**

Title compounds were prepared by using 4-(*N*-(4-(3-phenylacryloyl) phenyl)sulfamoyl)-3-*p*-tolyl-sydnone condensed with malononitrile and pyridine via standard procedure.

SCHEME-VI: **4-(*N*-(4-(4-(substitutedphenyl)-5-cyano-6-methoxypyridin-2-yl)phenyl)sulfamoyl)-3-*p*-tolyl-sydnone**

The title compounds were obtained by taking 4-(*N*-(4-(3-phenylacryloyl) phenyl)sulfamoyl)-3-*p*-tolyl-sydnone condensed with malononitrile and sodium methoxide.

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SECTION-III

CHARACTERIZATION

All the synthesized compounds of each class were characterized by thin layer chromatography, elemental analysis, infrared spectroscopy and some of the representatives by nuclear magnetic resonance spectroscopy.

SECTION-IV

BIOLOGICAL EVALUATION

All the synthesized compounds have been evaluated for their *in vitro* biological assay like antibacterial activity towards gram positive bacteria and gram negative bacteria. The biological activities of the synthesized compounds have been compared with standard drugs.

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